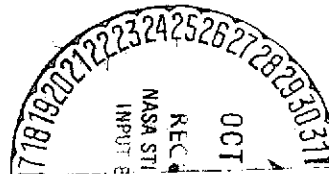


STUDY OF WEIGHTLESSNESS AND PERTURBATION OF THE RHYTHMS  
OF THE GASTROINTESTINAL SYSTEM OF ANIMALS AND HUMAN BEINGS

J. Thouvenot and C. Gaudeau

Translation of "Etude de l'agravite et des perturbations des rythmes  
sur le tractus gastro-intestinal chez l'animal et chez l'homme,"  
ESRO Space Biology Related to the Post-Apollo Programme,  
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16. Abstract Skin electrodes have been used to study the responses of the gastrointestinal system to weightlessness, with special attention to biorhythms. Future areas of study are outlined, including comparison of these responses to those of the cardiac, respiratory and nervous systems. A round table discussion between representatives of NASA and ESRO deals with the relative usefulness of immersion experiments, the problems of venous pooling and respiratory mechanics during space flight, psychological concerns, possible use of the astronauts to answer questions of cell biology (hair and fingernail growth, wound healing) and the problem of bacteria growth in space.			
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# STUDY OF WEIGHTLESSNESS AND PERTURBATION OF THE RHYTHMS OF THE GASTROINTESTINAL SYSTEM OF ANIMALS AND HUMAN BEINGS

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Laboratory for Advanced Research on Data Processing Methods,  
Department of Bio-Data Processing and Bio-Technology

I. Study of Fundamental Biology in Animals

II. Study of Human Biology with Application to Remote Observation

## Electrosplanchnography

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As a result of research on the electrical activity of the digestive organs of animals, the research group was able to show that it is possible to record bioelectrical signals of visceral origin in both animals and man with the sole use of skin electrodes (Thouvenot et al., 1968, 1970; Martin et al., 1969-70-71), that is, under completely normal physiological conditions. An analytic and synthetic study is being performed on the complex signals obtained, using processing methods (Gaudeau et al., 1969-70-71) strictly related to the data gained from experiments on animals (Thouvenot et al., 1970-71).

Thus a new methodology has begun to take shape: electro-splanchnography based on the acquisition, processing and comparison of experimental data, making it possible to monitor changes in the state of the digestive tract in relation to other systems: the cardiac, respiratory and nervous systems (Fig. 1).

## Study of Segmental Automatism

This area appears to be of considerable interest for the fields of biology and space medicine, since digestive problems which in

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\*Numbers in the margin indicate pagination in the foreign text.

practice may be surmounted in short-term flight become restrictive in long-term flight. Now, so far most of the work of Dietlein and Harris, Mack et al., and Whedon et al. (1966) on the physiology of the digestive system has dealt only with segmental mechanisms, and this methodology furnishes information on the situation of this entire system. Electrosplanchnography, on the other hand, makes it possible to determine the sequence of activities in various areas of the stomach, the small intestine, the colon, and even the bladder.

#### Relationships to the Nervous System. Method of Study

The prandial reactivity of the digestive tract to psychic stimuli appears to be dominant. This may be accurately evaluated by this method, from a distance if necessary. Psychic and visceral interactions in the area of affective reactions are already known. The research of Prof. Granpierre (see the report contained in this volume) has clearly indicated the significance of changes in intellectual capability under the effects of gravity.

It happens that sensory data of visceral origin (mechanical receptors, voluntary receptors) are disturbed and even eliminated in weightlessness.

Information on the role of these receptors under these conditions is still very imprecise.

#### Effects of Weightlessness

With reference to orbiting space stations, Dr. H.J. Smith ("The Use of a Space Station to Advance the Goals of Science") has defined one of the principal goals of the bioscientific program as determination of the biological effects of weightlessness.

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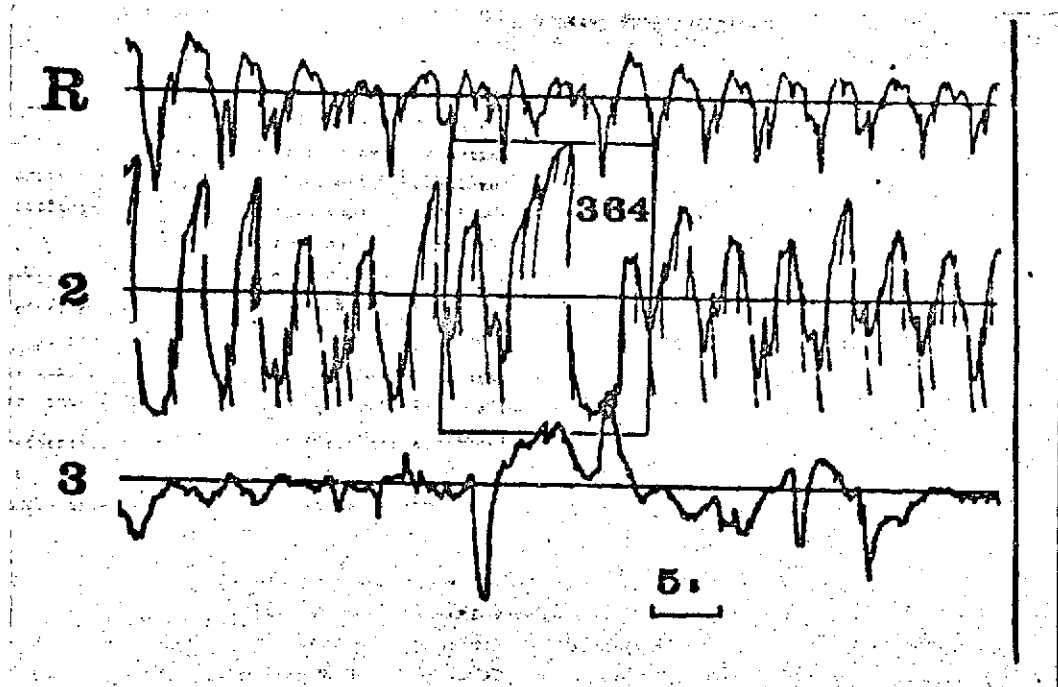


Fig. 1. Electrospianchnogram. From top to bottom:

(Z354)

- R: reference pneumogram obtained by gauge.
- 2: epigastric bipolar derivation in which a characteristic shape may be recognized (No. 364).
- 3: hypogastric bipolar derivation. Postprandial sequence.

Gravity plays a very important part in biological processes in our environment.

(a) Research on the reactivity of the digestive system to acceleration or variations in gravity should be expanded. The same is true of the suppressive effect of these stimuli produced by conditions of weightlessness. Intestinal motility, with its characteristic problems such as intestinal gas and sphincteral continence, merits special study due to its practical interest. (Dr. P. Arhan, et al.).

The research performed by the Group basically consists of

animal experiments performed at the Physiology Laboratory of the Tours College of Medicine (Prof. Thouvenot), notably including a study of segmental processes and absorption, and additionally, research on human beings (Arhan et al., 1971; Aron et al., 1962 and 1966; Martin et al., 1967, 1969-70).

(b) One process which may be considered to head the list for further research is that of intestinal absorption and its relationship to food or drug stimuli.

#### Digestive Absorption

The efficiency of digestive absorption is a major problem in aerospace biology dealing with prolonged flight. A great deal of research which has already been performed on the ground may be expanded to encompass long-term space experiments. Possible areas of experimentation include the reactions of the digestive system to acceleration, changes in position, food, drink, gastric fullness, urination and defecation under conditions of weightlessness.

Electrospalnchnography is one of the few means of recording the effects of pharmacological, atropinic, antiacidic and tranquilizing agents, stimulants, and others (aspirin, etc.) currently used without traumatizing the subject.

#### Biorhythms

In the environment of a space vehicle and in prolonged situations, electrophysiological signals may be used to study infradian, circadian and supradian rhythms.

In addition, with the use of skin electrodes, the electrospalnchnographic method offers a well-adapted mode of approach to the study of biorhythms, synchronized through meals and

nycterohemeral conditioning,

## Processing of Signals and Simulation of Adaptation Processes

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Finally, this research is based on a biomathematical methodology. This is due to the fact that the complexity of the signals collected necessitates appropriate processing methods.

It is conceivable that the processing methods may be more completely automated, not only for the analysis of observations, but also for studying infradian, circadian and supradian rhythmic behavior in interaction with the nervous system and all the conditions of the new environment, and, finally, for observation. In addition, the Biotechnology Department of the Laboratory for Advanced Research on Data Processing Methods (C. Gaudeau) is engaged more specifically in a study of the problem of processing, in collaboration with the Physiology Laboratory of the Tours College of Medicine (Prof. J. Thouvenot).

The research is concerned with:

(1) Coding and analog-numerical conversion of graphic and radiological recordings (research of Prof. de Possel) (Fig. 2).

(2) Pre-processing of signals and radiological images (determination of characteristic parameters of sequences or shapes).

(3) Processing of data:

-- filtering of disturbances by means of models (respiratory fluctuations, for example) (Fig. 3);

-- recognition of typical shapes and dynamic processes as a function of the environment for identification of the states of the various systems (Figs. 4 and 5);

-- detection of biorhythms (Cosinor program and spectral analysis);

-- finally, simulation of physiological systems, first, by a methodology based on sequential systems theory, and second, by the application of control theory (Fig. 6).

The basic importance of this simulation is that it can be used to provide a description of the mechanisms of adaptation of complex systems in response to an unusual environment.

This method is an integral part of the research project which cannot be dissociated from it, since it is designed to manifest the results.

## Projects

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### I. Study of Fundamental Biology (in Animals)

#### Objectives:

- The problems presented by weightlessness;
- intestinal absorption of water.

(1) Weightlessness reduces or eliminates the function of the gastric, intestinal and venous voluntary receptors of the mesenteric support system;

(2) The efficiency of intestinal absorption is a determining factor in study of the conditions for long-term flight with regard to water,  $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Ca}^{++}$  electrolyte, energy food, glucide, fat, protein and vitamin needs;

(3) The behavior of the digestive system in response to weight-



lessness and sequential digestive phenomena, hunger and appetite merit special attention in research on the effects of environment on rhythmic makeup;

(4) Study of the relationships between the brain and the digestive organs showed that the latter usually stimulate cerebral function to maintain alertness and to supply information on temporary mechanical stimuli (acceleration, deceleration).

#### Specific Studies

##### A. Study of Food Consumption and Digestive Rhythms in Rats

###### 1. Experiments on the Ground

Development and construction of a minimum-sized container with means to record the quantity of water ingested, food pellets

delivered, and feces eliminated in the course of prolonged tests. Actographic recording; temperature, hygrometry and pressure control; illumination system and food distribution system programmable.

###### 2. Experiments Under Weightless Conditions

Container with means for recording the same parameters as those indicated in Para. 1.

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Fig. 2. Digitization of an electrosplanchnogram trace by optical detector. Six sets must be digitized simultaneously, which requires a different exploration technique from the envelopes of curves technique.

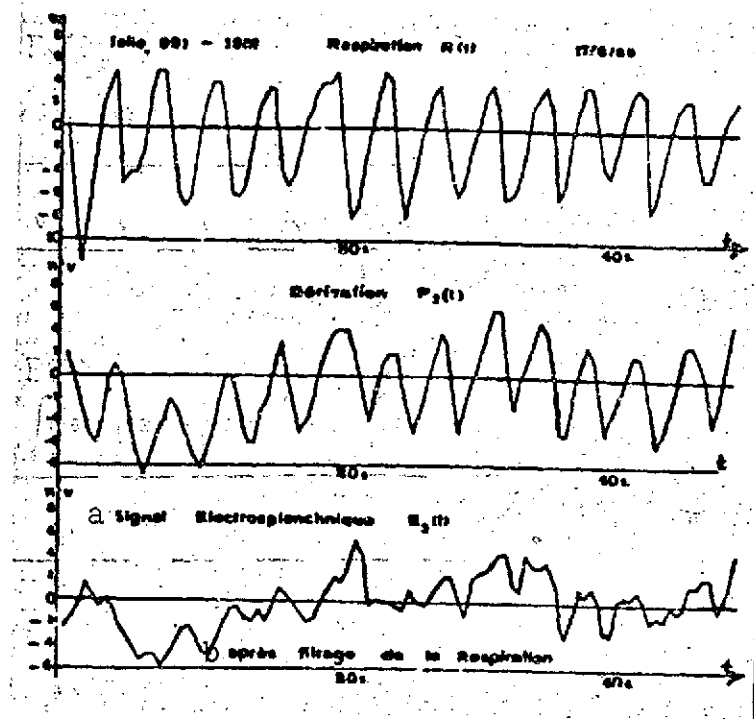


Fig. 3. Top to bottom:

$R(t)$ : respiratory fluctuations.

$P_2(t)$ : observed electrosplanchnic derivation.

$E_2(t)$ : electrosplanchnic signal computed by the residual method.

$$E_2(t) = P_2(t) - [0.598336 + 0.001964 R(t) - 0.31889 R(t-1) - 0.24328 R(t-2) - 0.105268 R(t-3) + 0.103099 R(t-4)]$$

Key: a. Electrosplanchnic signal.

b. After filtering of respiration.

The current prototype should be followed up by volume measurement devices capable of operating in weightlessness.

## B. Study of Derived Visceral Electrical Activity in situ and on the Surface

### 1. Experiments on the Ground

(a) Technical study of tolerance using skin electrodes and braided cables made of stainless steel, for example, to prevent their becoming corroded or being torn away by the animal; /361

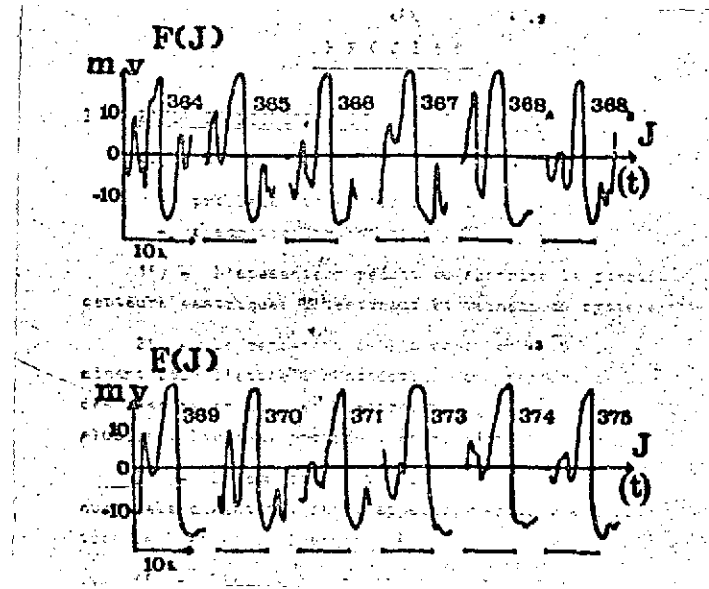


Fig. 4. Example of recognition of developmental processes in the ESG and of compression of data. A characteristic shape is detected by a filter and monitored throughout its fluctuations.

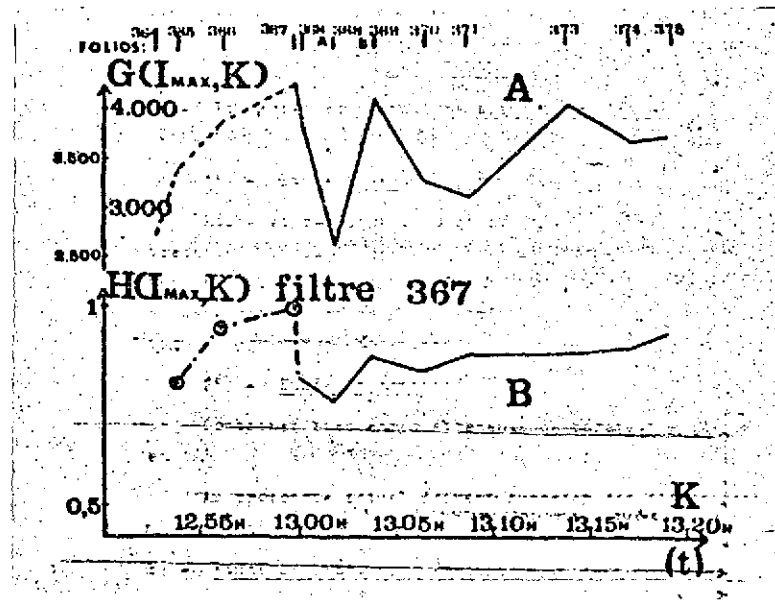


Fig. 5. The variations in the shape to be detected in comparison to a typical shape (filter 367) are described by a similarity function which makes it possible to trace the development of a physiological process as a function of the environment; this leads to valuable applications in the field observation.

(b) Subsequent tests deal only with surface derivations. The use of small transmitters in situ might solve the problems of connection;

(c) Processing of signals, study of sequential processes;

(d) Influence of acceleration on electrical activity.

## 2. Experiments under Weightless Conditions

### Equipment:

Eight electrophysiological channels, differential inputs 10 to 200  $\mu$ V.

Amplifiers (RC 0.7 to 7 sec) with asymmetrical outputs for connection with a remote control miniature magnetic recorder to start and stop sequences. The sequences may also be programmed by means of a local microprogrammer, which will preclude or limit the use of telemetering.

Sampled telemetering is desirable, on channels reserved for experimentation, for the purpose of observation and possible remote control operations.

## C. Testing of Absorption

### 1. On the Ground

Relationships between electrical activity and absorption of glucose,  $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Ca}^{++}$ . Rate of flow of segmental transits.

### 2. In Space Flight

(Possibility of experiments on oxygenated individual segments of the intestine under weightlessness.) (Crane technique; research of Mlle. Worbe, College of Sciences, Lyon).

### 3. Study of Gastric Ulcer

## II. Study in Human Beings

### 1. On the Ground

Study of digestive cycles in normal human beings by electrosplanchnography (visceral electrical activity by external derivation). Influence of materials ingested, food, water, and various types of medication.

Influence of changes in position, acceleration (centrifugal study project). Detection of various problems and types of discomfort (hiccups, nausea, cramps, anxiety.

Influence of psychoaffective and anxiogenic processes.

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### 2. Under Weightless Conditions (in Space Station)

Electrosplanchnograms recorded by sequence on magnetic tape and telemetering for observation.

It would be desirable to have eight channels available with inputs of 20 to 500  $\mu$ V, amplification RC 5 to 7 sec. Switching possible due to the slowness of variation; minimum sampling step 0.5 sec.

The following tracks would be necessary: one EEG track, six EEG tracks from which an ECG may be drawn under the observation conditions, and one P. neurography trackk

In addition, there should be one tape recorder track which the subject may use to note the sensations felt and the events occurring: impressions, anxiety, physical needs, urination, defecation, amount of urine and feces.

Future research might deal with the following problems;

Comparison with the state of the cardiovascular and respiratory systems (hemodynamic and respiratory changes related to changes in the state of the digestive system).

Comparison with the central nervous system:

- alertness and digestive state studied by EEG derivation
- forehead-vertex, for example.

- The aptitude for mental or physical work, the degree of initiative and the manual dexterity ~~will~~ be evaluated during flight and noted on magnetic tape.

The large amount of data which will be obtained presupposes methods of comparative analysis which, in some cases, might be performed in real time.

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Viôlette: I would like to thank Dr. Thouvenot for his very interesting report. Does anyone have any questions to ask on Dr. Thouvenot's report?

Question

(no mike): Have you noted any changes in the trace with age?

Answer: Yes, we have noted that the parameters of the trace change with age. In aged subjects, or even subjects 60 years old or older, the trace is significantly flatter. These are subjects who are completely healthy, whose appetite is completely normal, and who, nevertheless, show a flatter trace. Another example actually occurring in states of lack of appetite, even in marked states of anorexia: flat traces have been noted, and in mental anorexia, oddly enough -- this is a problem which does not concern us here, but it might be mentioned as an example -- in mental anorexia, the digestive tract does not react to psychic stimuli, and only when the condition is improved through psychotherapy and medication does the digestive tract begin to react. With the use of our method, when the trace is observed to change shape, a satisfactory prognosis is possible, and the subject begins to regain his appetite somewhat after three months. This shows quite well that it is possible to make predictions as to these much-disputed digestive rhythms. I feel that these problems of feeding are extremely important under space conditions.

Violette: We are going to try to throw out some possible ideas on space research. What we would like to have here is a "brain drain," that is, to get our brain cells working and pool our ideas. This is how I understand the purpose of this round table. Now, I am open to any system: if you feel that there might be a better technique to use in conducting this round table, in reaching definite goals and obtaining results -- I am completely open to the possibility of another system. So: does anyone have any suggestions to make as to procedure? If not, we are going to try to open up various subjects in the field of space medicine by asking you if these discussions have given you any ideas. Mr. Herzberg?

Herzberg: Yes, if possible, I would like you to define exactly what the purpose of the round table is. What should come of this round table? What are we looking for in this round table?

Violette: Research ideas! Since there are two types of participants: there are participants who are deeply involved in space medicine, and, on the other hand, there are individuals who have come, not as observers, but as actual participants, and for whom space medicine is not the original purpose, but who, since they have listened to the discussion, may have suggestions which have not occurred to the specialists in space medicine themselves. It therefore seems to me that this type of discussion can furnish new ideas. I would like something concrete to come of this analysis we are about to make. The important special

concerns of space medicine obviously include the absence of gravity. Does anyone have any research ideas which may have come to mind on this subject of weightlessness, in the light of what has been said yesterday and this morning?

Brieglieb: About a year ago I made a proposal to NASA for a sub- 4367 mersion experiment in respect to the problems of skeleto-muscular and blood circulation problems in respect to the adapting of man to weightlessness. In the background there is the g decision which is to be taken for the construction of orbiting laboratories, and I think the proposal we made is a reasonable one. We thought of adapting a skindiver-zoologist to a seawater environment, or a heated water environment over a long period of time, that is to say about four to six weeks, and have got results which others have tried to get from laboratory immersion experiments. When undertaking laboratory immersion experiments, it is necessary to ensure special protection for the skin of the subject under test, and there are great difficulties when carrying out these experiments in fresh water over long periods. As far as I am informed, it is not possible to protect a person's skin against infection for more than one week. It would therefore be necessary to use seawater, which is physiologically inert with respect to the skin, and this is not feasible in a laboratory because the seawater will attack the laboratory instruments. Another important point is the motivation of the subject, on account of which a subject is often unable to endure experiments of this kind over a long period. A further factor is that in laboratory experiments, the subject cannot have sufficient physical activity, whereas a man in open water

can have an amount of activity comparable to the activity he would exert in a space laboratory. Our proposal was to test a zoologist with strong motivations to live in water -- in which he can carry out various kinds of research, such as ecological research on sea animals -- and acclimatize him to subtropical or tropical water located in a suitable climate (no storm regions, etc.); and also, there should be a protection against sharks (NASA, for example, has a laboratory equipped with nets). With suitable arrangements it should be possible to adapt a man to life under water for several weeks and carry out sufficient tests on his reactions with respect to the near-weightless environment in water. When we submitted our proposal, we had a complete team prepared for this experiment: it consisted of two physicians, two zoologists and technical assistants. We submitted the proposal to the Marshall Space Flight Center, but it was rejected by NASA HQ in Washington. I think that Europe could renew the proposal for such an experiment to NASA and I should like to have comments both from ESRO and from NASA's representatives.

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Violette: I think I would like to ask Mr. Bernier what he thinks about this. Personally, I wonder if the value of immersion experiments at the present time is as great as it was a few years ago, since they have yielded up all the results they can give. Furthermore, there are also fairly serious differences between living in an aqueous medium -- since the viscosity of water is quite high -- and living in a gaseous atmospheric medium, the atmosphere of space capsules, where the subject is not in a viscous medium; this at any rate results in a strong difference in behavior. The prob-

lem of electrolytes is also involved. All in all, there are a great many differences. Nevertheless, for a given period of time this was the method of approach. Personally I wonder if large-scale tank experiments are not a little outmoded at present. This is my point of view as a physiologist and one who has followed the progress of space medicine since its beginnings. It may be that NASA and ESRO have a different opinion, and other participants in the hall may also have different opinions. So I would like to ask Mr. Bernier and Mr. Atlan if they have any response to give.

Bernier: Thank you, Mr. Chairman. I am going to take advantage of the fact that we have two experts from NASA here today who obviously know more about the status of what our efforts have been,, are now and will be in the future, in this field, to comment on your statement. I do not know whether Dr. White or Dr. Saunders is the best one to answer this, but maybe a short, justta short, position on what we are doing or not doing back in the States on this would be in order.

White: I think Dr. Violette has raised a very interesting and important question. One of our difficulties in using water immersion has been the fact that we had artifacts produced evidently by the water and the dif-  
ficulties in controlling pressures. We made sure that we had not imposed a problem of equipment to ensure that regulation of gases to the lungs, etc., was so sensitively controlled that it did not produce an artifact. I think we have gone more towards bed rest as our analogue even with its problems, primarily because the events, and the sequence and timing of events, that

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we have found with the bed rest are a better model in a time relationship to those we have observed in the varying length space flights. Now, in contrast, we do use water immersion, as I noted this morning, for training for those sequential events that take longer than 30 seconds which we can attain in a single trajectory. We found that in preparing for extravehicular activities, where men had tasks that took longer than 30 seconds and up to several minutes, the interlude, or rest period, between the various trajectories would produce artifacts of such magnitude that the training experience was suspect and that the time line of laying out the flight plan was suspect. I think that Prof. Grandpierre noted that in his presentation today we had some of the astronauts taking many minutes to do tasks that normally take in short simulation, seconds to do. I think this is a very complicated problem. It is the fact that there is a continuity element here and water immersion seems to be the best element of doing that simulation. I do think, though, that we have seen dramatic results in water immersion and it took us several years to sort out what was due to what we were looking for in the analogy to weightlessness versus what was due to the artifacts produced by the water itself.

Brieglieb: I should like to reply that adaptation to life under water can still be expected and that in any case such an experiment will be of great value and will be more meaningful with respect to function of blood circulation and functions of the skeleton than simulation experiments could ever be. I think it is worthwhile finding out whether the adverse side effects of immersion -- such as those found by Prof. Gauer in Berlin after ex-

periments of short duration -- are really very serious or whether a body is able to react sufficiently against them. A lot of money is spent on experiments aimed at making space flight safer and the amount of money needed for our experiment is relatively small compared to the great benefits it might bring. I am not a physician, and I do not want to go into details, but I think my general philosophy is right.

Violette: I would like to interject something here if I may. I think we 370 really are losing sight of our purpose, which was to see what might be applicable to space medicine. We are no longer completely within the purpose of this round table, which is actually to draw from the earlier discussions anything which might be directly usable in space. I feel there was some justification in talking about subaquatic medicine, but this is really the field of subaquatic research, and I do not think that it offers any great benefits from a space standpoint. Frankly, I believe that at present there are budget requirements both for NASA and for ESRO, and we should think not only about researchers, but also organizers, that is, the cost of the financial operations. I know that you might say, "Well, what are we really doing? Are we using biology in the service of space or space in the service of biology?" This, however, is a slightly different philosophical problem, and with your permission we will forego it for the present; we are going to find ourselves in endless discussions and will still be sitting here tomorrow morning tossing the ball back and forth.

Atlan: I would like to take the occasion of the question which was asked me to make it very clear that in no

way do I represent the position of ESRO, in that there is no ESRO position in regard to problems of biology. With reference to the specific problem which has been raised here, I am completely unequipped to make any statement, and can therefore give no answer as to my personal position. In general, the position or positions of ESRO now actually depend on you to a large extent. The very reason ESRO has held this conference is to try to draw out a few ideas on how to respond to a NASA invitation to participate in the Post-ApollorProgram. I know that in organizing a conference of this type, it is necessary to move away somewhat from already existing findings, research which has already been performed, and this is not necessarily the best method. It was for this reason that we felt it imperative to hold two completely open sessions, one on medicine, today, and the other, which will be tomorrow, on biology. During these sessions those individuals who have not had a chance to express their opinions initially, even if they are not specialists at all, will be able to express their ideas or thoughts. Now I know that some have already stated privately that they were deeply shocked by the way in which space research has been conducted up to the present, at least in regard to biology and medicine, since it appeared that in the majority of cases, it was not so much problems of medicine or biology themselves which were considered, but the universe, that is, an attempt was made to draw biology and medicine toward application in space. I think the time has come -- at least in regard to medicine -- for these individuals to express in public what they have been able to express in private.

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Violette: All the same, I would like to say a few short words in defense of NASA, even though I am theoretically neutral. After all, during the last ten years the main project has been to put men on the moon, and it may be said that NASA has succeeded. It was also necessary to solve human problems, and perhaps in the details, one might find occasion to find fault, but it should be said that these problems have been solved in general, and that this already constitutes a highly satisfactory result in the field of physiology, and I feel that it does deserve credit. What country was it that put men on the moon, if not the one that funds NASA? We do after all owe NASA a debt of gratitude, and I think that any quibbling on this point would be relatively futile. Prof. Donato?

Donato: I will try to follow the suggestion of our Chairman that we try to come up with some ideas. I do not have, I must say, any specific ideas, but during the last two days I have been comparing within my mind what has been done so far with the problems we are faced with in our laboratory and what part of our work could benefit by this approach; a sort of cross-fertilization could thus take place. Now, the comments I am going to make refer specifically to the cardiovascular and respiratory problems. One line of investigation on which we have been very active in the last ten years is the control of pulmonary blood volume. I apologize if I have to say a few words just to be sure of being understood. Pulmonary blood volume, we know now, plays a sort of permissive role in the function of the ventricle, the adequate function of which demands that an adequate amount of blood is present in the pulmonary circulation. Now this amount of blood is controlled

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by various factors, the most important of which seems to be the venous return, at least in normal conditions. Of course, it is quite different in cardiac patients, but in normal conditions, the main controlling factor is the venous return. There are methods now, currently used, which permit estimating very simply the pulmonary blood volume and pulmonary mean transit time, and we have been following the various factors that control this volume. Now, when I heard that the problems of venous pooling seem to bother the astronauts after their return to earth, it immediately came to my mind that it would probably be of some interest to find out what is the behavior of pulmonary blood volume and what is the behavior to pulmonary blood time, which would probably provide a very simple way of testing indirectly the extent of venous pooling. There is no direct way nowadays of measuring venous pooling by various indirect and very approximate methods, particularly when venous pooling is subclinical, but this might provide some important information and of course this would be quite an important return from this sort of study to the understanding of controlling pulmonary blood volume. That is one point and if the Chairman prefers it, I could stop for a moment before moving to the second point if you want to discuss this point.

White: Well my only comment to Dr. Donato is that I agree with him that this is an area that we need to investigate. I also agree with you that our problem has not been lack of interest but lack of available techniques with 373 the accuracies that would satisfy us. I would also note one other element in the problems of venous pooling. From all the tests and indications we have in flight, and these are gross, we have not done, as you

know, the lower body negative pressure or any other test which would indicate that the pooling is an event of at least overt observation. For the men in orbit, to date (even during the 14 days and from what we can gain from the Soviets in their 18-19 day Soyus 9 flight in orbit), there was no problem, they were more than adequate. They did not detect increases in pulse as an indirect way of showing a deconditioning to a severity, or a magnitude, that would produce a problem for the men as they functioned in orbit. It only became an overt thing and a measurable thing of significance after the return. And so I think, it may be a little bit more complicated as we could not use a tilt table which is the sort of test we have always used on the ground. This is the reason we went to lower body negative pressure, hoping that sometime we would be able to get it into flight. We will not be satisfied until we actually do the measurements of the venous compliance, the venous pooling, the venous return and the very general conditioning of the whole cardiovascular system of which the returnal blood is one element in this, which of course, as you say, does influence pulmonary return or efficiency of pulmonary ventilation in the lung, but we think it is a little more complicated and we have not seen it in flight. Incidentally, I would recommend Dr. McCally to you in this area, because he has done much work before he took his year here in Europe with you in the early studies of using bed rest and lower body negative pressure, and I think he is probably very well versed to speak on this subject.

McCally: Dr. Donato, there is an interesting relationship between your comments and the fact that everyone speaks of

of science in the service of space, or space in the service of science in the particular area of the regulation of volume distribution, in which you have mentioned the pulmonary circulation as one example. It is, I think we all realize, one major mechanism involved in cardiovascular responses to space. In this particular instance I think our technology, namely space medicine, has outstripped our science, as you and your laboratory, as you well know, have no good method for the measurement of continuous volume distribution and of time histories of volume distribution changes. I would like to make the same measurements in space to answer the same kinds of questions, but here again, we have been able for centuries to measure pressures, have, for a few years, been able to measure flow, but we are still unable to measure volume effectively in a continuous fashion and therefore we cannot expect space to provide us with answers for which our present science does not give us the tools. So I think the answer there lies not in space but in our laboratories here at home to develop in this case a good method for the measurement of volume distribution. In this case, the problem is one that space cannot serve science and science could serve space by developing this particular technology. /374

Donato: I do not think I made myself too clear -- I said there are methods -- unless I did not understand your comments -- there are existing simple methods to measure blood volumes that can be used repeatedly, and are used repeatedly, and that are not too traumatic because they simply involve the venous injection of a radioisotope, and you know that one can use very short living radioisotopes now with extremely low radiation

to the patient and this way one may obtain repeated measurement of pulmonary blood volume. Here in the discussion today, I took one decision that I am certainly going to see what happens to this pulmonary blood volume in relation to flow in patients, in normal patients, during prolonged bed rest, because I am curious to find out whether in this condition there is a reduction of pulmonary blood volume. I think that, for instance, if one could do this set of measurements, which is very simple, in people returning from space on whom you make this sort of observation, you could obtain this sort of information -- and that by existing techniques!

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White:

I should note, though, that the measurement can be made, but it is not simple because you remember that total blood volume is reduced and electrolytes have been changed. So unless you can do all of these as a complex of pulmonary blood volume and venous pooling, all these must be put into their context and I think that is the complexity to which Dr. McCally was referring. It is a complex of events of which the result is the appearance of the cardiovascular system. I think that you must admit that these elements do and have shown change and are changing and also admit that we do not know if these are changes which come to a level of stabilization after a period of time appropriate for the weightless environment or whether they are progressive and how all these various aspects of fluids, electrolytes, muscular conditioning, efficiency of the muscle as far as oxygen uptake and maintenance of oxygen efficiency are concerned, interplay together. The measurements we can use as a complex to tackle these various elements and how these

play together in the space condition is the thing, I think, that Dr. McCally was alluding to here. It is very difficult and I think we are at the point in time in saying that we do recognize the complex is one thing to measure and to interpret it is another thing, and I think this is where, in interpreting it, we outstripped ourselves. I think this is -- the reason I want to be sure that I leave it this way in the discussion -- an area where the biological sciences can make a real contribution and you have the experts in Europe who can do this. I would like to encourage them to put this complex to work and sort out new techniques and the integration of these new techniques to tackle this complex problem. Maybe then it will lead to an experiment.

Violet: I stated that the gross phenomena are known; these are /376 details which are much less well known, since the sensations which the astronauts experience, the sensations of fullness in some parts of the body,, certainly indicate changes in blood distribution. It is certain that the volume receptors discovered by Gauer function in weightlessness, since increased diuresis may be observed during the initial moments of flight. Due precisely to these changes and the redistribution of the blood volume, which moreover does not become distributed correctly, it follows that there must be some intervention by the organism at that time. I believe that what should be sought is primarily a simplification of methods and a means of placing them within the range of astronaut physicians. Again, the phrase "space in the service of biology, biology in the service of space" was used earlier. If methods are successfully simplified

to work in the Skylab, certainly it will be possible to transfer these methods which have been simplified for work in Skylab to the ground, and the experiments will thus have benefited human medicine. But what is necessary is the desire for simplification, since there is obviously very little room in space laboratories, by definition, and moreover, it will not always be possible to send physicians or teams of physicians into space; this points to the need for orientation. We should not attempt to conceal the problems, but should orient them, and I believe that this orientation of space research will be beneficial to human medicine and to human functional experimentation, if not on a short-term basis, at least on a long-term basis. Consequently this is a satisfactory line of research. Dr. Donato?

Donato: I would just like to add one comment. As far as I understood the problems we are discussing here, I did not think you were just looking for experiments to be carried out in the Skylab laboratory, but I thought that you were also looking for experiments to be performed on earth in normal laboratories that could help /377 to interpret changes occurring either in flight or after the return of the astronauts. This is the sort of information that I think could be usefully investigated to interpret some of these changes. I was not actually proposing experiments to be carried out in the Skylab laboratory.

Violette: I believe that is actually what is desired.

Jacquesin: Currently, laboratory research has for some time been directed toward the development of techniques of

creasing versatility and adaptability to all environments. We have performed experiments on respiratory mechanics in virtually all possible environments and at all altitudes. Our experimental subjects have included laboratory subjects and completely untrained subjects, ranging from a physiologist who was a native of the Andes, on whom we were able to perform respiratory mechanics tests, and most recently, one or two months ago, we were able to perform tests on divers who had reached the world record depth of 520 m; these tests were performed with a type of equipment which could be used under all conditions and exploiting the respiratory mechanics under satisfactory conditions. We also exposed the subjects to high gravity using a centrifuge. For good reason, the only environment which we were unable to use was the weightless environment. We are currently developing a large number of experiments, and especially, a large number of increasingly simplified and adaptable instruments, and I believe that with a little more effort we will be able to make devices which can be used under space laboratory conditions available to respiratory mechanics researchers. In another connection, I would like to refer to a NASA document (the Blue Book), which gives the following as a priority problem which must be solved: the effects of prolonged weightlessness on the mechanics of respiration in normal subjects, where the forces of gravity normally interact with the respiratory muscles and the elastic forces of the thorax and lung. As I have tried to show in this discussion, all the means necessary to perform this type of experiment are available at present, together with the capacity to complete these experiments by producing a reaction with changes in pooling between the infra- 7378



thoracic and intrathoracic parts of the blood. At the present time, therefore, with some additional effort it will actually be possible to provide researchers with technical solutions which will furnish an answer to the priority question posed by NASA.

Violette: I would like to thank Dr. Jacquemin for what he has pointed out. I believe that it is at least interesting that he has made proposals on the methods he is using at NASA. I believe that they now will be passed along. In any case, the point is an interesting one. I believe Dr. Herzberg has something to say.

Herzberg: With reference to the behavior of astronauts, I believe that with longer flight times, psychological experiments might be performed. I am referring to batteries of projection tests to determine how gravity gives human beings a certain way of seeing themselves and how the absence of gravity might transform this self-image and the image of the body, for example. We know, for example, that in hospitals the details of the body image of long-term patients undergo a transformation simply by reason of their horizontal position. It would be interesting to see how weightlessness acts from a psychic standpoint on the basic psychological makeup of astronauts; this might perhaps give some feedback on the states of mind of individuals who are not astronauts.

Violette: Some answers have already been obtained from a psychological standpoint, on the concept of verticality, for example. The concept of verticality in weightlessness appears to be completely relative, in contrast to the concept of verticality on the ground,

and I believe that there are other phenomena which have already been examined. I feel that this line of research will be followed initially and should be followed, because in another connection, the behavior of a subject during either a space mission or an orbital mission is nevertheless fairly special. But what specifically did you want, since reports by astronauts have already shown that a great many answers can be given, and there are astronauts, whether from the U.S. or the Soviet Union, who have remained for long periods of time -- up to two weeks -- in weightlessness, and they have made reports on their return. If you can be somewhat more specific... /379

Herzberg: What I am thinking of, more precisely, is projection tests. Rorschach tests, for example, or something of that nature, which would be made every day to monitor changes in the astronauts.

Violette: I believe this question should be handed over to Dr. White and the NASA representatives. In addition, I believe that tests of this sort have been made. Would there be any value in considering a program in this direction?

White: In response, I think we should note that the study of the crew does not start with projection tests when they are in orbit. The projection or the study of the individuals must begin back during the consideration as to what criteria should be used in selection, and this is a continuing program throughout their training period and really ultimately leads to the selection of the men to make up the crew that goes on a given flight. I would just like to note, having participated in the

selection program dating back from the original United States astronauts, that we had changed our minds as to the personalities and the types of people that we were looking for. It seems such a short time ago, that is one decade, that to form the original group of astronauts, we were looking for people who are the ones that I think I can characterize by saying they are self-sufficient men; they are the ones who are by the fact that they survive, live=exciting, to us who are more mundane people, occupations, the fact that they /380 survived in this, meant that they had successfully led these kinds of exciting and thrilling existences. This meant though that they were also self-sufficient as they had planned to fly alone, with the possibility that they would be out of contact with the ground. Now after that initial group, there has been a progressive change away from that type of personality, which was selected with the idea that, now, they must work as a team, that they must be capable of reacting as a unit, that personalities must be complementary if possible or if the mission or the objectives of the mission insisted upon it. Now you have raised a very interesting and I think a very important area for the future, because I believe that we are at the next major milestone in the problems of personality and group composition. We are talking about a small community with a command system or structure to be established -- the interrelationships of the crew, one crewman to another and her in turn with the crew as an entirety -- with the shuttle and the ability to bring up new members and take some away back home again, the objective being scientific products in orbit, the goals of flying being to maximize the scientific return on each flight. This means that perhaps people who are not necessarily compatible with

each other are the right ones to go for the specific objective of the scientific role. So I think the problem of behavior is again, as I said to Dr. Donato, a very complex one as I see it. I am not sure at this point that we are intelligent enough to know whether we can select or try to only select out in our community of scientists those who just physically or emotionally could not make the trip -- to allow the breadths to be opened up so that most can make the trip and do their job to the scientific endeavor and return safely. In other words, we would not want to take a man who would be a hazard to himself or to the rest of the crew, but I think as near to that limit would be desirable. Now I do not know whether we need testing in orbit -- perhaps -- or whether there are other kinds of social indicators that we could use as to whether man is moving into a dangerous area. There are personality changes, so maybe the test would be the most sensible way and it is perhaps why we need to perform tests. I would ask you, though, to look at it from /381 the point of view as to whether the tests need to be done with that kind of frequency. Now I am speaking of this not as a scientist looking at the scientific experiment, but from the point of view of a practical flight surgeon who has the sort of responsibility of seeing that on the ground the machinery continues and that the operation continues to fly. If it takes the testing that you are suggesting, such as Rorschach or others, on a daily basis, naturally that should be done, but I think one of the really difficult tests is to look at the situation and ask ourselves as biological scientists, what those tests need to be, the content of them, the frequency and the interrelationship of those tests as regards the rest of the astronaut's

daily activities so that we can harvest the total information. Now I will say to you that one of the silent experiments that will now be talked about or will be looked at very seriously in Skylab is of trying to start this important area for 28 days and 56 days and to see whether we can begin to identify, from a practical, medical point of view, recognizing that we are taking scientists, but very highly selected scientists, and a test pilot, as our crewmen here, knowing full well that when we come to the Space Station or the shuttles with their modules, we are going to want to move to a less selective population, so we are hoping to harvest this not as an experiment but as an education for ourselves to do a better job. I think the important conclusion I want to leave is that we must do this if we are to be successful in going space flight. Now, whether it is a Rorschach test or other kind of indicator I do not know. I think this is an area where such a group of minds as this can be very helpful to us. Giving us guidance in this area would be extremely helpful and would be something that you could contribute to us. I think, by the way, it also will help because the space kind of small population is a problem that we all deal with in our daily lives as well; so I think there is a byproduct here again for mankind right here on the ground. I think most of the work can be done on the ground.

Violette: I believed that Mr. Herzberg has found Dr. White's response satisfactory. I think -- in fact, I am almost sure -- that the main factor for a team of astronauts at the present time is "team spirit." There is always a leader in a team, and then there are

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others who must accept the presence of the leader and help him, and all this is a question of satisfactory comprehension. I have the impression, however, that this has been researched, since the NASA representatives responded to these concepts very quickly. Actually, one need only read the newspaper to see, for example, the spirit of cooperation of a man like Michael Collins, who, while two other members of the team landed on the moon, agreed to remain in orbit around it and in short, to stop just before the last step and not be allowed to go down. I feel that it is a totally admirable quality for a man to agree to watch his team members walk around and be the first lunar explorers and to have to be the one to stay behind -- but indispensable, nevertheless. I believe that if NASA succeeds in developing behavioral tests, a means of "measuring" behavior enabling it to locate men of this type, this will also be useful from a medical standpoint and from the standpoint of use on the ground, since after all, only teams will be exploring the moon, and teamwork by two, three or more individuals is extremely important.

Budinger: To return to the suggestion of the Chairman that we get some new ideas, I would suggest perhaps using astronauts to learn something about cell biology. Now, there are some very simple ways of learning something about growth in men even after a few weeks in space, and I would ask Dr. White, or perhaps best Dr. Saunders, to reply to three questions: the first is why not wound the astronaut and see how well he heals; the second is why do we not weight the fingernails and measure the fingernail growth before, during and after; and the third is how about hair? -- not only hair weight, and

hair growth, but activation analysis on hair, and this is my attempt to weld cell biology and basic science to the astronauts in their present mission configuration.

Saunders: I did not look around, but I assume that was Dr. /383  
Budinger. First of all on the question of fingernails, I guess we could do this. From the standpoint of growing hair, the astronauts, as I recall all their excursions, have come back with beards and they grew their hair. For the typical mission, Borman and Lovell, for the 14 days they grew beards but they insisted on being shaved when they came back, and they were shaved on board the aircraft carrier or the helicopter that docked them back. Therefore, after all, this is an important thing for them, when they are meeting the press and whether anybody thought of what you said from the standpoint of collecting that hair and trying to measure it and determine whether keratinization was taking place and whether there was any increased growth.

McCally: Could I make a guess? I can make a guess as to why it was rejected due to a recent communication in Science, which correlated beard growth with sexual deprivation and expectation, and I suspect the astronauts might not want their sexual ideation revealed by their beards.

Saunders: Well, as Dr. White has just pointed out, it has been discussed. I did not know this because I was not that involved with the astronauts and probably it is a very good idea. I do not know what we would find out of it. Do we have a hypothesis that we could suggest that

there is going to be a change, or is this weightlessness going to change the growth rate of the conformation of the keratin molecules or whatever it is that is involved in this? I think that we have got to advance a hypothesis first of all and have some good thoughts behind it and have an understanding, as Dr. McCally has pointed out, to see if this is related in any way to some other psychological barrier or problem, and then, if it is a good idea and it is acceptable to the scientific community, it would be worthwhile looking at -- of course the astronaut has to cooperate.

Budinger: The main question with respect to hair growth would include activation analysis. It would include activation analysis along the whole length of the hair shaft, and this can be done. It is a way of measuring the trace elements and electrolyte deposition in the hair as it grows, and it is feasible -- it is just observational science. One can carry forth two hypotheses: one, there will be a change, two there will be no change, and carrying these original hypotheses one can look at the rate of growth. It is very difficult to do a 30-day nail growth, linear growth and weight growth on astronauts before and after they come back from the mission, and I think it is a problem of logistics. The major point of my questions is that if we want to see some effect in a few days or a few weeks of free fall on the human system response and involved cells, then we should look for some amplifying aspect of the system which means we have to pulse it, and my suggestion is, why not control wound healing or control wounding of astronauts; a secondary aspect of this question is, do we draw blood and will we start

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drawing blood in free fall?

Saunders: Well, Dr. White pointed out yesterday that samples will be taken, put on a slide and prepared and stored for analysis when they return. From the standpoint of wounding an astronaut, I do not think I would go along with that. However, we do have experiments at the Ames Research Center. Dr. Haymaker is probably familiar with the problem of regeneration of the liver in rats. That experiment was proposed many years ago and is still under development. We just have not had an opportunity to fly it. I would not go along with wounding an astronaut because of the stresses and everything else that he has up there -- I think this is just imposing another one. Let him take care of an animal or a tissue that has been wounded and see how it regenerates.

Violette: I feel that I should come to the support of Dr. Saunders to say that with regard to individuals such as astronauts, first, there is no point in "stressing" them, and second, it should be extremely difficult /385 for physicians, even for physicians in whom they have every confidence, to convince them to take a large number of samples, because, since they have had extremely intensive training, since they have a great many things to do, there is no point, in my opinion, -- and this would be the case for any country -- for physicians to tire them too much. They might carry out these tasks patiently, but I feel that this patience could very easily be exhausted.

White: I think we did not perhaps answer Dr. Budinger's statement completely in regard to the wound healing. I

think this wound healing question is a very valuable one and needs to be done. I would second Dr. Saunders' suggestion that I would like to see a well-controlled experiment using some other tissue besides that of our crew. I think this needs to be done in a very basic way first. I am sure that as time progresses we will have the opportunity to observe a real-live wound, accidentally produced, in a crewman and will have the opportunity to study healing characteristics in a human. However, I do believe that it is important enough that this area should be considered very thoroughly and an experiment designed to study the the concept of wound healing. Experiments designed should be performed both on the ground and under the conditions of space, as best we can do, with the ultimate experiment perhaps flown. I would like to do that in non-astronauts first. I would like to have that information so that when the first injury does occur, I might have a reasonable chance of knowing what to expect, because there are some hypotheses which would indicate that wound healing may be much more serious in a non-gravity area.

Atlan: There is something I just do not understand: what are the differences which are expected between animals and men and between mammals and men with respect to this phenomenon? Are there any differences?

Budinger: Of course the hypothesis that one entertains with re- 7386  
spect to this is one which has to do with gradients and diffusion in regard to regenerating tissues, and what you are saying is that you would expect the same thing to go on if there are some changes in an animal, which are foreseeable, but I do agree that it is best

to start with an animal.

Bock: I would like to change the topic. I want to know what is the philosophy of NASA at the moment concerning the microbial environment in prolonged missions?

White: Dr. Saunders has volunteered me again; I notice that he has been doing that ever since the conversation started! The microbial area, I believe, is a really fruitful area for some very, very serious thought. Proposals have been made, and there is just recently one experiment that has been approved to go aboard one of the last flights of Apollo: to take a series of cultures of well-known organisms, expose them to the lunar environment on the surface without vacuum -- in other words, they will be in everything but vacuum -- and to return this material to observe whether there are mutations, changes or survival in the cultures. Now, in addition to this, one of the operational procedures that will be aboard Skylab is that there will be, as part of the medical support unit, a rather extensive microbiological testing capability to include culture media and to include the capability of doing antibiotic sensitivity testing in the event that an astronaut becomes ill and we want to treat him rather than return him. In addition to this, there will be, as a standard procedure, early in the flight at a medium period in the flight and late in the flight, samples taken throughout the spacecraft and these samples and swabs will be cultured and returned for study after the mission. This is done from the very practical point of view of trying to ascertain whether we have a scrub-down point when the next crew comes up. As a way of cleaning up the lab, since the bacteria

will have been left, it will have been exposed to a near vacuum period between the crew visits. But this 1387 microbiological area is one on which I think we can really do some very good thinking, because we have become very smug in our understanding of bacteria today on the ground under 1 g and we have not looked at bacteria from the point of view as to whether they can or will change in the various aspects of the vehicle operation, and in the event that they are out in vacuum, as to their survival capability and their modification or mutation that might be imposed by space environmental stresses. Ittthink this is an area where there is a lot of work which needs to be done and I think it is going to take some very good ingenuity to get this program put together so that it makes sense and I think it is a lot of work for everybody in this area.

Saunders: This is to supplement what Dr. White has said, that we did have some studies with germ-free animals and what we were interested in is finding out whether there was any microbial exclusion or whether there was any re-combination or anything else with these bacteria. For example, the germ-free animal was injected and inoculated with bacterium A and nothing happened to this animal. In the first case, you can see what the transmissibility was and how fast A grew in the animal that was germ free. The second point was to take A here and B here and see what happened when we mixed these two animals; the one containing A and the one containing B, and see if you have a predominance of AB or BA or whether they were not affected, and these studies are still continuing. There is also another one that is under consideration at the Manned Space

Center: 30-day or longer chamber runs with animals to see what happens to their microbial populations, and the important thing is that assuming this is a harmless or an innocuous bacterium here and that this is a potential pathogen, this was the big concern, and the indications -- the preliminary indications of the germ-free test -- are that the potential pathogens seem to take advantage of the less hostile organisms and seem to dominate the population.

Violette: Thank you, Dr. Saunders. I am sorry that it is time /388 to think about giving up the hall, since this has been a very interesting discussion and we already have a few indications for research, since it was interesting to see the ideas presented, and then, on the basis of these ideas, to discuss research performed in European laboratories which may support the work being done by NASA. Four lines of research have already been pointed up. I will give them in random order. First, there was Dr. Donato with his research on the pulmonary blood volume, which may produce valuable results: it appears to me that some collaboration might be useful here. There is also the work of Mr. Jacquemin, which could furnish significant results both from the standpoint of space research and from that of medicine per se. Finally, there are the broad options: bacteriology, histology and anatomopathology. I feel that European laboratories might also be used in these areas. The problem of healing I believe is fairly well known, but the theory, but there may not yet be sufficient data on it, and at present, it deserves to be re-examined with modern technical methods, which will furnish new results and perhaps new orientations for research. In any case, the problem of healing will be

of use for the astronauts, and it will also be of use in related areas; I feel that one of the objectives of NASA is to furnish results relating directly to the astronauts, but also results in related areas, to look for spin-off. The field of bacteriology also seems to me to be of prime importance, but I have purposely avoided bringing up radiobiological problems, since this will be a topic of the discussion tomorrow. I believe that we already have several options, and there are perhaps possibilities Both from the standpoint of European collaboration with NASA and from the more general standpoint that this European collaboration with NASA will produce spin-off studies in the field of medicine. I personally feel that there has been considerable spin-off from space medicine, in the area of miniaturization, if nothing else, and these medical spin-off results would not have occurred without the enormous financial backing. The goal has been to obtain results pertaining to the /389 astronauts, but these medical results researched by NASA for the astronauts have been beneficial to mankind, if I may state it in that way. Consequently, I feel that we owe our gratitude to NASA and to the U.S.; we should also try to press forward. I would like to close on this note: let us forge ahead, working together with the same team spirit as that of the astronauts. In any case, thank you for your cooperation. I myself have learned a great deal, and I feel that this has been a learning experience for all of us; if there is anybody who hasn't found this to be the case, there have at least been people here with information to offer. There has been mutual benefit, a mutual give and take, and this in itself is remarkable for a scientific meeting.